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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/905,370 | 07/12/2001 | Preeti G. Lal | PF-0802 US | 3719 |

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| EXAMINER |
|---|
| SLOBODYANSKY, ELIZABETH |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/905,370 | LAL ET AL. | |
| | Examiner | Art Unit | |
| | Elizabeth Slobodyansky | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3-7,9,11,13-15,27,28 and 46-53* is/are pending in the application.

4a) Of the above claim(s) *13-15,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,9,11,46-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

The amendment filed February 24, 2003 canceling claims 1 and 2, amending claims 3, 11, 46 and 48-51 and adding claims 52 and 53 has been entered.

Claims 3-7, 9, 11, 13-15, 27, 28 and 46-53 are pending. Claims 13-15, 27 and 28 are withdrawn. Claims 3-7, 9, 11 and 46-53 are under consideration.

### *Specification*

The specification is objected to because it contains references to the tables that are presented as separate entities. There is "brief description of the tables" on page 7. If Applicants consider said tables as drawings they should designate them as "Figures" and they will be subjected to Draftsman review. If Applicants intend to have tables that are not drawings they should insert them before claims with the description preceding them, for example.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 13, lines 26, 29, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification refers to "GenBank ID g181382" on page 22, line 18, and in Table 2 where it appears ""GenBank ID 181382" is intended. Correction is required.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-7, 9, 11 and 46-53 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants disclose a nucleic acid sequence (SEQ ID NO: 2) encoding the amino acid sequence of SEQ ID NO: 1. Based on a sequence homology, the polypeptide of SEQ ID NO: 2 is sought to be a cytochrome P450 variant ("CYTPV-1", page 3, lines 8-9, for example). A cytochrome P450 belong to a superfamily comprising several families of enzymes that usually act as terminal oxidases in P450-containing monooxygenase systems and are involved in many biological processes (specification, page 1). Cytochrome P450 enzymes widely differ in substrate specificity. Humans produce hundreds of cytochrome P450 enzymes and each cytochrome P450 is expected to have a specific substrate(s) and function. Thus, the utility of being a cytochrome P450 is a generic utility. Applicants did not assert any specific utility for a

polypeptide of SEQ ID NO:1 and a DNA encoding thereof. Applicants teach that activity of CYTPV can be demonstrated using as substrates aniline or testosterone (pages 70-71). However, the cytochrome P450 having more than 99% identity to SEQ ID NO:1 (P450 1A2, Hayashi et al., EP 0644 267 A2, form PTO-892 mailed November 19, 2002) shows no activity towards testosterone (pages 12-13; page 15, Table 1). Thus, Applicants needed to carry out further research to identify the specific function of a polypeptide of SEQ ID NO:1 or the nucleic acid sequence of SEQ ID NO: 2 at the time they filed their application. In fact, the specification does not provide any evidence of an enzymatic activity for the protein encoded by SEQ ID NO:2. Therefore, as disclosed, a protein of SEQ ID NO:1 is an uncharacterized protein. In view of this, an isolated protein of SEQ ID NO:1 has no specific, substantial or well-established utility.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-7, 9, 11 and 46-53 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following rejections would apply even if the utility of SEQ ID NOs:1 and 2 were established.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 49-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 11 and 49-50 are drawn to a naturally-occurring polynucleotide variant that is at least 95% or 98% identical to SEQ ID NO:2. Therefore the claims are directed to a genus of naturally-occurring variants, or alleles, of SEQ ID NO:2.

Naturally occurring nucleotide sequences having at least 95% identity to SEQ ID NO: 2 encode variants the function of which **may or may not be altered**. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles

is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of others.

Thus, a naturally-occurring polynucleotide variant that is at least 95% or 98% identical to SEQ ID NO:2 encoding a polypeptide having undisclosed function lacks sufficient written description needed to practice the invention of claims 11 and 49-50.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID NO:1 and fragments consisting of 750 contiguous nucleotides of SEQ ID NO:2 or nucleotides 843-1582 thereof, does not reasonably provide enablement for a DNA comprising 750 contiguous nucleotides of SEQ ID NO:2 or nucleotides 843-1582 thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 51-53 comprise two embodiments: first, DNAs encoding variants having the function of SEQ ID NO:1 and second, DNAs encoding variants lacking the P450 function of SEQ ID NO:1 and having undisclosed functions.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

With regard to the first embodiment, fragments comprising 750 contiguous nucleotides of SEQ ID NO:2 or nucleotides 843-1582 thereof are highly unlikely to encode cytochrome P450 activity and the specification does not teach otherwise. The specification does not support the broad scope of the claims which encompass all modifications and fragments of any sequence that comprises any of the above fragments of SEQ ID NO:2 because the specification does **not** establish: (a) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; (C) a rational and predictable

scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptide structure having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Furthermore, the second embodiment of claims 51-53 encompass DNAs encoding polypeptides having no known functions. While it is known in the art and is taught in the specification that the fragments themselves can be used as probes, the claims encompass DNAs of unknown structure and unknown homology to SEQ ID NO:2 comprising said fragments and encoding inactive variants. The specification does not teach how to use said inactive variants. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The state of the art does not allow the predictability of the properties based on the structure. Therefore, one skilled in the art would require guidance as to how to use a DNA of unknown homology to SEQ ID NO:2 comprising 750 contiguous nucleotides

of SEQ ID NO:2 or nucleotides 843-1582 thereof and encoding a polypeptide of undisclosed function in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 9, 11 and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite % identity. The claims are deemed to be indefinite in view of the prior art that has homology that is very close to the claimed homology. It is impossible to make an accurate comparison of the two highly homologous sequences without knowing the program and the algorithms and the parameters that are used.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 49 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Jaiswal et al.

Jaiswal et al. (GenBank accession Z00036, form PTO-1449, references 3, 18, 24) teach a DNA encoding human cytochrome P3(450) that is 93.6% (best local similarity of 97.5%) identical to SEQ ID NO:2, a vector containing it and a cell expressing thereof. The rejection is made in view of the indefiniteness of the claims, *supra*.

***Response to Arguments***

Applicant's arguments filed February 24, 2003 have been fully considered but they are not persuasive.

With regard to the written description, it appears that applicants argue the enablement. They argue "specific assays to measure cytochrome P450 activity are disclosed in the Specification at, for example, page 70, line 21 to page 71, line 14". Regardless of the applicability of the activity assays disclosed in the specification and discussed in the utility rejection, *supra*, in relation to claims 11 and 49-50, there is no description of a single naturally occurring sequence having at least 95% identity to SEQ ID NO:2 that encodes a polypeptide with the function other than the function of the polypeptide of SEQ ID NO:1 nor are such sequences known in the art.

With regard to the enablement rejection, Applicants argue that "one of skill in the art would know how to use the claimed polynucleotide fragments as hybridization probes or PCR probes to detect the presence of a polynucleotide comprising SEQ ID NO:2" (page 17, last paragraph). This is correct with regard to the fragment consisting of 750 contiguous nucleotides of SEQ ID NO:2 or nucleotides 843-1582 thereof. However, the claims are not limited to such fragments and encompass DNAs of unknown structure comprising said fragments and encoding unknown function.

With regard to the 102(b) rejection over Jaiswal et al., it is maintained because of the indefiniteness issues discussed *supra*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

May 16, 2003